

30 May 2016

Re: Docket EPA-HQ-OPP-2016-0205

I write in response to the request for comments on Docket EPA-HQ-OPP-2016-0205 regarding application 89668-U from the MosquitoMate, Inc to register ZAP Males (*Aedes albopictus* males infected with *Wolbachia pipientis*) as a pesticide.

I am a molecular biologist and geneticist and I was one of the first to apply molecular techniques in plant biology commencing in the 1970s. I have been involved in the regulatory issues around modern genetic modification – GM – since the early 1980s, when I served on the NIH Recombinant DNA Advisory Committee. I was also one of the authors of the 1987 National Academy of Sciences (NAS) White Paper titled: “Introduction of Recombinant DNA-Engineered Organisms into the Environment: Key Issues.

As such, I recently reviewed an application to release male mosquitoes genetically modified by the company Oxitec (now a subsidiary of Intrexon) to pass a lethal gene to offspring as a mosquito control measure. The application had been submitted to the FDA, which has undertaken to regulate such mosquitoes as a “new animal drug.” As part of the regulatory process, Oxitec was required to submit an Environmental Impact Assessment, which was available in its entirety for public comment, as was the application for experimental release of mosquitoes.

By contrast, application 89668-U from the MosquitoMate, Inc to register ZAP Males (*Aedes albopictus* males infected with *Wolbachia pipientis*) as a pesticide is not available for examination, although public comment on the application is requested. I therefore base my comments on examination of the relevant literature.

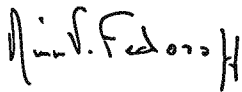
The use of *Wolbachia*-infected mosquitoes to control mosquito populations is in its experimental infancy. The basic observation is that a *Wolbachia* infection spreads and takes over an insect population by a variety of mechanisms, but particularly by cytoplasmic incompatibility, such that eggs produced in an incompatible cross fail to hatch. Suppression of a local insect population is based on the release of *Wolbachia*-infected males only. However, the females are not genetically sterile, hence sorting is most likely done by size and visual inspection, neither of which is 100% effective.

The possibility remains that the introduced strain will simply replace the native strain through amplification of the offspring of matings between *Wolbachia*-infected males and females, however infrequent. Suppression will likely be short-term and simple takeover of the population by *Wolbachia*-infected *A. albopictus* will be the long-term outcome.

Hence both an environmental impact assessment that addresses the probability of population replacement based on actual data is essential, a concern arising from the results of recent studies (Maurizio et al.). Essential as well are data on the ability of the

Wolbachia-infected population to acquire and transmit relevant diseases, including dengue, West Nile Virus, and particularly the Zika virus.

Yet it appears that the EPA is about to approve unrestricted release of large numbers of infected insects without either an EIA, studies on its safety, or a back-up plan should the population be fully converted to the released *Wolbachia*-infected type or should other unexpected adverse effects surface.

A handwritten signature in black ink, appearing to read "Nina Fedoroff". The signature is written in a cursive, somewhat stylized script.

Nina Fedoroff, PhD

Evan Pugh Professor Emerita, Penn State University, University Park, PA

nvf1@psu.edu